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Original Research

Permanent Pacemaker Use in Transcatheter Aortic Valve Replacement: Real World Experience from the National Inpatient Sample

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Abstract

Background: Transcatheter Aortic Valve Replacement (TAVR) is associated with conduction abnormalities requiring permanent pacemaker implantation (PPMI). Data regarding predictors for PPMI following TAVR is scarce.

Methods: This is a retrospective study utilizing the 2017 National In-Patient Sample (NIS). Patients who underwent TAVR and PPMI during the same admission were identified using appropriate ICD-10 codes, as were patients with left bundle branch (LBBB), right bundle branch (RBBB), and first-degree AV delay (AVB). Patients were split into two groups based on PPMI. The groups were compared using univariate and multivariate analyses after adjusting for age, gender, race, comorbidities, insurance status, and Charlson comorbidity index (CCI). Secondary outcomes included factors influencing length of stay (LOS) and total charges incurred.

Results: In 2017, 54,175 (57.6% males) patients underwent TAVR. There were 8,067 patients with LBBB, 2,402 with RBBB, and 2,905 with AVB at baseline. A 4170 total of patients (55.2% males) required PPMI. Patients requiring PPMI were older (80.5 vs 79.6 years, p=0.001). On multivariate analyses, baseline RBBB, LBBB, hypertension (HTN), CCI 2, and CCI >/=3 predicted PPMI (aOR 4.82, p<0.001; aOR 1.63, p<0.001; aOR 1.21, p=0.013, aOR 1.53, p=0.022 and aOR 1.46, p=0.031 respectively). On multivariate analyses, patients who underwent PPMI had significantly higher LOS (aOR 2.18, p<0.001) and incurred higher total charges (USD 278,000 vs USD 204,920; p<0.001).

Conclusion: In this cohort, RBBB, LBBB, HTN, and increased CCI predicted PPMI after TAVR. Further studies are required to corroborate our findings.

Keywords: TAVR, Permanent Pacemaker, National Inpatient Sample

Introduction

Over the past two decades, transcatheter aortic valve replacement (TAVR) has revolutionized the field of cardiology offering a minimally invasive procedure to manage aortic valvular disorders. TAVR is now approved by the US Food and Drug Administration (FDA) in patients with any level of surgical risk profile [1-5]. Since the first TAVR implant in 2002, multiple clinical trials including the PARTNER trial have evaluated its clinical use in a variety of patient settings.

Conduction system injury after TAVR requiring permanent pacemaker implantation (PPMI) is a known complication of aortic valve interventions. Despite ongoing improvements in TAVR delivery systems, conduction abnormalities that require PPMI remain a common development following TAVR due to the proximity of the atrioventricular conduction system to the aortic root. Pre-procedural conduction abnormalities such as right bundle branch block (RBBB) and left bundle branch block (LBBB) have been associated with increased PPMI and mortality. The available literature regarding the impact of conduction abnormalities and PPMI on long-term patient outcomes is still conflicting [6]. Numerous patient- and procedure-related factors have been cited as being responsible including advanced age, male gender, atrial fibrillation, small left ventricular outflow tract, preprocedural or intraprocedural conduction disorders, calcification of aortic and mitral annulus, balloon pre-dilation, and depth of prosthesis implantation [7,8]. As TAVR is moving to younger and lower-risk patient populations, we sought to identify/clarify the risk factors for PPMI after TAVR in a large real-world database.

Methodology

Study Design and Variables

This was a nationwide retrospective study of all adult patients hospitalized in 2017 to undergo TAVR in the United States. Patients who underwent TAVR were selected from the Nationwide Inpatient Sample (NIS) database which is part of databases developed for the Healthcare Cost and Utilization Project (HCUP). Weighted, it extrapolates more than 35 million admissions nationally. Patients were divided into two groups based on the need for PPMI. Patient and hospital-level data are categorized based on a variety of socio-demographic and geographic parameters in addition to the ability to use ICD10-CM and procedure codes to identify patients.

Statistical Analysis

Analyses were performed by using STATA version 17. Univariate logistic regression analysis was used to calculate unadjusted odds ratios (ORs) for the primary and secondary outcomes with a second logistic regression model being built using only variables that were associated with the outcome of interest on univariable regression analysis at $P< 0.2$ to obtain an adjusted OR. Patients with missing information for any of the variables in the regression analyses were excluded. Proportions were compared by using Fisher's exact test, and continuous variables were compared by using the Student t-test. All P values were two-sided, with 0.05 as the threshold for statistical significance.

Results

Patient Characteristics

Of the >35 million discharges included in 2017, 54,195 met the inclusion criteria of undergoing TAVR. Of the patients who underwent TAVR, 4,170 (7.7%) required PPMI during the same hospital admission. Of the study population, 2,402 (4.4%) patients had RBBB, 8,067 (14.9%) had LBBB, and 2,905 (5.4%) had first-degree AV delay (AVB) at baseline.

Patients were then divided into two groups based on the need for PPMI (see Table 1). Patients in the PPMI group were older (80.5 vs 79.6 years, p=0.001), more likely to have a history of hypertension (HTN) (51.2% vs 47.2%, p=0.03), and with lower female patients in both groups (44.8% vs 42.2%, p=0.51). Other patient and hospital characteristics such as race, Charlson

comorbidity score, annual income quartile by zip code, primary insurance, hospital bed size, hospital region, hospital teaching status, diabetes mellitus (DM), chronic heart failure (CHF), chronic kidney disease (CKD), obesity, pulmonary hypertension (HTN), obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD), and smoking were not significantly different between the two groups. The proportion of patients with baseline LBBB, RBBB, and AVB was higher in the PPM group. (Figures 1a, 1b)

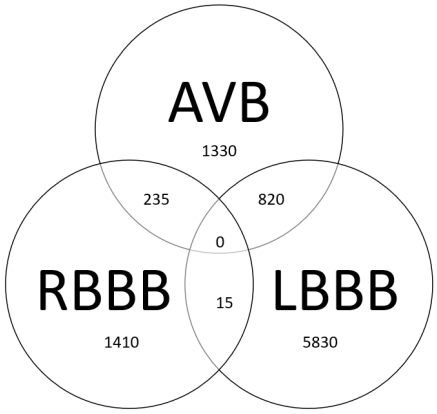

Figure 1a: Distribution of Conduction Blocks in Non-PPM Group

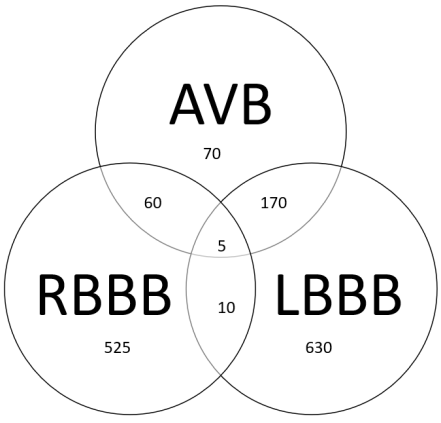

Figure 1b: Distribution of Conduction Blocks in PPM Group

Predictors of PPMI

On univariate analyses, age, HTN, smoking, higher CCI score, income quartile, Western geographic region, primary insurance, and hospital bed size were found to be predictors of PPMI in addition to RBBB, LBBB, and AVB. (See Table 2).

On multivariate analysis, after adjusting for potential confounders, RBBB was found to significantly predict PPMI post-TAVR (aOR 4.82, p<0.001) as did LBBB (aOR 1.63, p<0.001). Female gender and age did not influence PPMI post-TAVR (aOR 0.99, p=0.925 and aOR 1.01, p=0.065 respectively). HTN and higher CCI (2 or >/=3) significantly pre-dicted PPMI post-TAVR (aOR 1.21, p=0.013, aOR 1.53, p=0.022 and aOR 1.46, p=0.031 respectively). (Table 3 and Figure 2)

Secondary Outcomes

Length of Stay and Total Hospital Charges

Patients who underwent TAVR and PPMI during the same admission had over twice as longer a length of stay as compared to those who did not require a PPM (6.3 days vs 4 days; aOR 2.18, p<0.001). In concordance with a longer length of stay and additional procedure, patients who required PPMI post-TAVR also incurred significantly higher total hospital charges when compared to those who did not undergo PPMI (USD 278,000 vs USD 204,920; p<0.001).

Discussion

In this large nationwide observational study comparing TAVR patients based on the need for PPMI, we found that approximately 8.3% required PPMI during the same admission. In our study, the presence of [1] right bundle branch block (RBBB), [2] left bundle branch block (LBBB), [3] hypertension, and [4] increasing Charlson comorbidity index score predicted PPMI after TAVR while male gender and increasing age were not predictive. This analysis examined a contemporary, population-based cohort that included all prosthesis types. PPMI post-TAVR was associated with a longer length of stay and more expensive hospitalization. Prior data by Fauchier et al showed that among patients who underwent TAVR between 2010-2019, 27% required PPMI post-TAVR with a mean follow-up of 1.2 years with the majority requiring it within the first 30 days [9]. Mazzella et al reported that amongst 62,083 patients who underwent TAVR; 6,817 (11%) underwent PPMI with the

majority occurring during the same hospitalization, and only a tenth occurring during a subsequent hospitalization [10].

increased need for PPMI during the index admission. Our study also showed pre-existing LBBB to confer almost

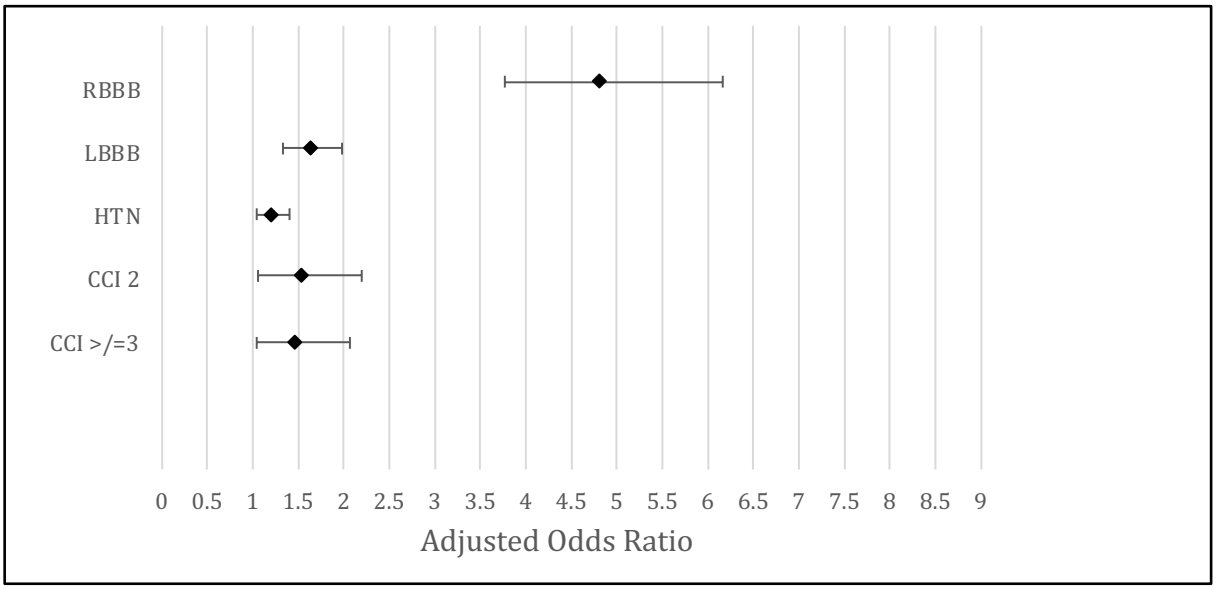

Figure 2: Forrest Plot showing results of Multivariate analysis for Variables with p <0.05

Conduction disturbances are a well-known complication of AVR due to the anatomical adjacence of the aortic valve to the conduction system. PPMI occurs in roughly 1 in 6 patients within 30 days after TAVR and is influenced by the depth of implantation, device type, individual patient anatomy, and pre-existing conduction abnormality [11,12]. Post-TAVR conduction abnormalities resulting in PPMI range from 1 in 12 (6.50%–10.0%) for the Edwards SAPIEN balloon-expandable valve (BEV) (Edwards Lifesciences; Irvine, CA) to 1 in 4 (4-40%) for the Medtronic CoreValve self-expanding valve (SEV) (Medtronic, Inc.; Minneapolis, MN) [13-17].

Preexisting RBBB, low depth of implantation, and use of SEV have been identified as common and consistent risk factors for PPMI [18-25]. Prevalence of RBBB in the general population ranges from 0.5% to 1.5%, increases with age to 2.2%, and is observed more commonly in men [26,27]. Patients with prior RBBB who undergo TAVR can suffer damage to their left bundle branch (LBBB) or His-bundle running along the membranous septum which can then result in complete heart block (CHB). In our study, pre-existing RBBB predicted almost a 5-fold a 2-fold risk of PPMI with almost 20% of patients in the PPM group having a pre-existing LBBB. Our study reaffirms pre-existing LBBB as a significant predictor for PPMI as suggested by prior studies [28]. Fischer et al looked at the impact of LBBB outcomes after TAVR [28]. They performed a multicenter study of 4,513 patients undergoing TAVR over 12 years and excluded those with preexisting RBBB or prior PPMI resulting in a sample size of around 3,400 with preexisting LBBB being present in 398 patients (11.7%). Preexisting LBBB was associated with a significantly increased risk of early (< 30 days) PPMI compared to those without LBBB (21.1% versus 14.8%; aOR 1.51, CI 1.12-2.04) [28].

Although the mean age of patients who required a PPMI was statistically higher than those who did not require one, numerically they were less than 12 months apart. Our study did not show that increasing age was a significant predictor of the need for PPMI post-TAVR. Existing literature has been conflicting regarding age as a factor. Recently, Ullah et al's large-scale study showed that there was no statistically increased rate of PPMI post-TAVR in patients aged above 80 when compared to

those under 80 years old although the older group had a 19% higher PPMI rate [29]. We hypothesize that given the numerically small difference in age between our study groups and the correction for other confounders, age no longer remained a significant predictor.

We also report a lack of significant gender differences among Post-TAVR PPMI rates. A recent meta-analysis of 46 studies from 2011-2019 by Ravaux et al showed a 10% lower PPMI post-TAVR in females at 30-day post-TAVR (aOR 0.9 [0.84-0.96], p=0.002) [30]. The lower rate of PPMI in other studies has been attributed to favorable baseline characteristics [31]. However, data from WIN-TAVI showed the volume of Right coronary cusp calcium as an important predictor of PPMI in women which we cannot account for in our study [32]. We hypothesize that the higher amount of endocardial fibrosis and abnormal collagen in men, and more favorable left ventricular (LV) remodeling in women compared with smaller LV outflow tract size lead to equivocal PPMI rates immediately post-TAVR in our study cohort [33-36] after correcting for comorbidities.

The impact of PPMI requirement after TAVR has been controversial, with one study by Fadahunsi et al demonstrating a significantly increased hazard of 1-year all-cause mortality after PPMI [37] while another study by Siontis et.al reporting no negative outcomes [7]. The negative impact of PPMI post-TAVR can be attributed to asynchronous activation of ventricular segments, reduction in cardiac output from atrioventricular dyssynchrony, regional septal hypo-perfusion, left-sided valvular dysfunction induced by right ventricular pacing and progressive ventricular remodeling [38-41].

As confidence in TAVR procedures increases, patients are being discharged sooner after TAVR [42]. Shortened hospitalization results in the potential for worse consequences due to late identification of AV block, which can present with syncope or sudden cardiac arrest. Unfortunately, our ability to predict heart block within a few days remains limited. There exist some differences between the 2013 European Society guidelines which recommend a more conservative approach allowing for the resolution of the transient block before PPMI while the 2020 ACC consensus recommends temporary pacing initially before committing to PPMI for conduction blocks post-TAVR [43,44]. A recent study employed atrial pacing immediately post-TAVR to predict the need for permanent pacing within 30 days and concluded that if AV conduction functioned without prolonging PR and dropped P waves with right atrial pacing up to 120 bpm, the rate of PPMI dropped by over 90% at 30 days [45].

Our study showed that PPMI resulted in significantly higher LOS and hospital charges. This is intuitive given the need for an additional procedure post-TAVR. There exists limited data on the impact of PPMI on healthcare resource use or costs. A retrospective analysis by Ahmad et al among 382 patients who underwent TAVR over 5 years between Dec 2012 to March 2018 showed PPMI resulted in significantly higher costs on an average of 10,213 USD (p=0.04) [45].

Limitations

Our study is a retrospective study using the NIS dataset, which includes only administrative data. Some limitations inherent to this database include non-uniformity of coding and missing patients who get PPMI at a later admission following TAVR. Given the observational nature of this study, there always remains the possibility of residual confounding. Causality is impossible to determine. However, the results from current data are important to provide a benchmark for future studies. Finally, this study focused on total charges during index presentation and did not include additional costs that were incurred post-discharge and at subsequent readmissions. However, the above limitations are unlikely to affect the primary purpose of the study.

Conclusion

Patients with pre-existing conduction abnormalities (presence of RBBB, LBBB) are at risk for further AV node injury following TAVR. Careful pre-procedural planning should factor these variables in the choice of valve, and the planned depth of valve placement. Identification of new conduction abnormalities post TAVR and optimal timing of PPMI are important issues that also need to be addressed. RBBB, LBBB, HTN, and a higher CCI score were identified as significant predictors for PPM implantation in this study. Minimizing the need for PPMI is only gaining importance as TAVR is increasingly chosen in younger and healthier patients.

Further prospective studies are needed to identify high-risk patients to predict the need for PPMI following TAVR to optimize outcomes while driving down costs and reducing the length of stay.

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Annex:

Table 1: Patient Characteristics Between Non PPM Group and PPM Group. Abbreviations: N: Sample size

Variable	Non-PPM Group N = 50025	PPM Group N = 4170	p-value
Women (%)	21,130 (42.2%)	1,870 (44.8%)	0.51
Mean Age (years)	79.6	80.5	0.001
DM	23,612 (16.8%)	705 (16.9%)	0.96
HTN	1145 (47.2%)	120 (51.2%)	0.03
CHF	25,913 (51.8%)	2,114 (50.7%)	0.59
CKD	16,408 (32.8%)	1,389 (33.3%)	0.74
Obesity	11,056 (22.1%)	963 (23.1%)	0.46
Pulmonary HTN	8,654 (17.3%)	788 (18.9%)	0.28
OSA	7,754 (15.5%)	717 (17.2%)	0.24
COPD	14,257 (28.5%)	1,222 (29.3%)	0.63
Smoking	20,160 (40.3%)	1,555 (37.3%)	0.1
RBBB	1,801 (3.6%)	601 (14.4%)	<0.001
LBBB	7,254 (14.5%)	813 (19.5%)	<0.001
1st Degree AV Delay (AVB)	2,601 (5.2%)	304 (7.3%)	0.03
Race			0.59
White	43,722 (87.4%)	3,636 (87.2%)	
African-American (AA)	2001 (4%)	184 (4.4%)	
Hispanic	2,302 (4.6%)	213 (5.1%)	
Charlson Comorbidity Score			0.18
0	2,751 (5.5%)	184 (4.4%)	
1	9,105 (18.2%)	672 (16.1%)	
2	10,505 (21%)	930 (22.3%)	
>/= 3	27,664 (55.3%)	2,385 (57.2%)	

Annual Income by Zip			0.093
0-43999	10,605 (21.2%)	788 (18.9%)	
44000-55999	13,207 (26.4%)	1,018 (24.4%)	
56000-73999	13,157 (26.3%)	1,126 (27%)	
>74000	13,057 (26.1%)	1,243 (29.8%)	
Primary Insurance			0.08
Medicare	45,573 (91.1%)	3,895 (93.4%)	
Medicaid	700 (1.4%)	21 (0.5%)	
Private	3,602 (7.2%)	242 (5.8%)	
Other/Self pay	150 (0.3%)	8 (0.2%)	
Hospital Region			0.36
NE	11,706 (23.4%)	1,055 (25.3%)	
Midwest	11,456 (22.9%)	1,017 (24.3%)	
South	16,959 (33.9%)	1,384 (33.2%)	
West	9,905 (19.8%)	717 (17.2%)	
Hospital Bed Size			0.22
Small	3,402 (6.8%)	204 (4.9%)	
Medium	9,705 (19.4%)	855 (20.5%)	
Large	36,918 (73.8%)	3,111 (74.6%)	
Hospital Status			0.30
Teaching	44,772 (89.5%)	3,786 (90.8%)	
Non-Teaching	5,253 (10.5%)	384 (9.2%)	

Table 2: Univariate Analyses with Unadjusted ORs for PPM implantation. Abbreviations: OR: Odds Ratio

Variable	OR	p-value	Confidence Interval
Age	1.01	0.001	1.005-1.02
Female Gender	0.95	0.51	0.82-1.10
DM	1.005	0.957	0.84-1.21
HTN	1.17	0.027	1.01-1.35
CKD	1.03	0.744	0.88-1.19
Obesity	1.06	0.455	0.90-1.25
CHF	0.96	0.591	0.83-1.12
OSA	1.13	0.243	0.92-1.37
COPD	1.04	0.628	0.89-1.20
Smoking	0.88	0.100	0.76-1.02
Pulmonary HTN	1.11	0.284	0.91-1.36
RBBB	4.47	<0.001	3.52-5.7
LBBB	1.43	<0.001	1.17-1.74
AVB	1.44	0.029	1.04-1.99
Race (Compared to White)			
AA	1.12	0.515	0.79-1.57
Hispanic	1.10	0.552	0.80-1.52
Annual Income by Zip (Compared to <43,999)			
44,000-55,999	1.03	0.755	0.84-1.28
56,000-73,999	1.15	0.185	0.94-1.4
>74,000	1.28	0.024	1.03-1.58
Charlson Comorbidity Score (Compared to 0)			
1	1.1	0.628	0.75-1.60

2	1.33	0.113	0.94-1.88
>/=3	1.29	0.143	0.92-1.81
Hospital Region (Compared to NE)			
Midwest	0.99	0.905	0.78-1.24
South	0.91	0.392	0.73-1.13
West	0.80	0.149	0.60-1.08
Teaching Hospital (Compared to Non-teaching)	1.15	0.301	0.88-1.51
Hospital Bedsize (Compared to Small)			
Medium	1.46	0.095	0.94-2.26
Large	1.40	0.115	0.92-2.1
Insurance (Compared to Medicare)			
Medicaid	0.35	0.036	0.13-0.93
Private	0.79	0.134	0.58-1.08
Self Pay/other	0.79	0.754	0.18-3.42

Table 3: Multivariate Model Showing Adjusted ORs of Variables predicting PPM placement after TAVR

Variable	Adjusted OR	p-value	Confidence Interval
RBBB	4.82	<0.001	3.77-6.16
LBBB	1.63	<0.001	1.34-1.98
AVB	1.09	0.615	0.78-1.53
Age	1.01	0.065	0.99-1.02
Female	0.99	0.925	0.85-1.16
HTN	1.21	0.013	1.04-1.41
Smoking	0.89	0.137	0.76-1.04
Annual Increase by Zip (Compared to <43,999)			
44,000-55,999	1.02	0.836	0.82-1.27
56,000-73,999	1.12	0.286	0.91-1.39
>74,000	1.18	0.136	0.95-1.48
Charlson Comorbidity Score (Compared to 0)			
1	1.26	0.238	0.86-1.86
2	1.53	0.022	1.06-2.20
>/=3	1.46	0.031	1.04-2.07
Hospital Region (Compared to NE)			
Midwest	1.03	0.811	0.81-1.31
South	0.99	0.911	0.78-1.24
West	0.92	0.565	0.68-1.24
Hospital Bedsize (Compared to small)			
Medium	1.43	0.09	0.94-2017
Large	1.36	0.121	0.92-2.01